2.0 ABSTRACT

Malignant mesothelioma is a tumor of the pleura for which there is no satisfactory treatment. It is almost universally fatal, regardless of the stage of the tumor at the time of diagnosis. Current treatment modalities include surgery, chemotherapy, and radiation therapy, although in some series none of these modalities is superior to no treatment at all. Because of the dismal prognosis for patients with malignant mesothelioma, a new mode of treatment is desperately needed. A promising area of research into the treatment of various malignancies is gene therapy. Recent studies have demonstrated the utility of exposing tumor cells to cells transduced to express the Herpes simplex virus gene for thymidine kinase (HSV-TK). By virtue of their expression of HSV-TK, the transduced cells are rendered susceptible to the antiviral drug, ganciclovir (GCV). Nearby tumor cells are killed by a so-called bystander effect. In this protocol we propose a Phase I trial to study the safety and determine the maximal tolerated dose of an HSV-TK-transduced ovarian cancer cell line (PA1-STK cells) infused into the pleural cavities of patients with malignant pleural mesothelioma, followed by systemic administration of ganciclovir. The hope is that administration of ganciclovir will result in killing of the transduced ovarian cancer cells as well as the nearby malignant mesothelioma cells. This is a standard dose-escalation protocol.